



Books

□ 1: NM_075774. Caenorhabditis el...[gi:25150522]

Links

LOCUS	NM_075774	1473 bp	mRNA	linear	INV 12-JUL-2003
DEFINITION	Caenorhabditis elegans Suppressor/Enhancer of Lin-12 SEL-12, SUPpressor of Multi-vulva phenotype SUM-1, presenilin, membrane protein facilitator of Notch receptors signaling (50.0 kD) (sel-12) complete mRNA.				
ACCESSION	NM_075774				
VERSION	NM_075774.2 GI:25150522				
KEYWORDS	.				
SOURCE	Caenorhabditis elegans (worm)				
ORGANISM	<u>Caenorhabditis elegans</u> Eukaryota ; Metazoa ; Nematoda ; Chromadorea ; Rhabditida ; Rhabditoidea ; Rhabditidae ; Peloderinae ; Caenorhabditis.				
REFERENCE	1 (bases 1 to 1473)				
AUTHORS	Lakowski,B., Eimer,S., Gobel,C., Bottcher,A., Wagler,B. and Baumeister,R.				
TITLE	Two suppressors of sel-12 encode C2H2 zinc-finger proteins that regulate presenilin transcription in Caenorhabditis elegans				
JOURNAL	Development 130 (10), 2117-2128 (2003)				
MEDLINE	<u>22554535</u>				
PUBMED	<u>12668626</u>				
REFERENCE	2 (bases 1 to 1473)				
AUTHORS	Kitagawa,N., Shimohama,S., Oeda,T., Uemura,K., Kohno,R., Kuzuya,A., Shibasaki,H. and Ishii,N.				
TITLE	The role of the presenilin-1 homologue gene sel-12 of Caenorhabditis elegans in apoptotic activities				
JOURNAL	J. Biol. Chem. 278 (14), 12130-12134 (2003)				
MEDLINE	<u>22552452</u>				
PUBMED	<u>12556527</u>				
REFERENCE	3 (bases 1 to 1473)				
AUTHORS	Eimer,S., Donhauser,R. and Baumeister,R.				
TITLE	The Caenorhabditis elegans presenilin sel-12 is required for mesodermal patterning and muscle function				
JOURNAL	Dev. Biol. 251 (1), 178-192 (2002)				
MEDLINE	<u>22301592</u>				
PUBMED	<u>12413907</u>				
REFERENCE	4 (bases 1 to 1473)				
AUTHORS	Eimer,S., Lakowski,B., Donhauser,R. and Baumeister,R.				
TITLE	Loss of spr-5 bypasses the requirement for the C.elegans presenilin sel-12 by derepressing hop-1				
JOURNAL	EMBO J. 21 (21), 5787-5796 (2002)				
MEDLINE	<u>22299931</u>				
PUBMED	<u>12411496</u>				
REFERENCE	5 (bases 1 to 1473)				
AUTHORS	Li,J., Pauley,A.M., Myers,R.L., Shuang,R., Brashler,J.R., Yan,R., Buhl,A.E., Ruble,C. and Gurney,M.E.				
TITLE	SEL-10 interacts with presenilin 1, facilitates its ubiquitination, and alters A-beta peptide production				
JOURNAL	J. Neurochem. 82 (6), 1540-1548 (2002)				
MEDLINE	<u>22242246</u>				
PUBMED	<u>12354302</u>				
REFERENCE	6 (bases 1 to 1473)				
AUTHORS	Francis,R., McGrath,G., Zhang,J., Ruddy,D.A., Sym,M., Apfeld,J., Nicoll,M., Maxwell,M., Hai,B., Ellis,M.C., Parks,A.L., Xu,W., Li,J., Gurney,M., Myers,R.L., Himes,C.S., Hiesch,R., Ruble,C.,				

Nye, J.S. and Curtis, D.

TITLE aph-1 and pen-2 are required for Notch pathway signaling, gamma-secretase cleavage of betaAPP, and presenilin protein accumulation

JOURNAL Dev. Cell 3 (1), 85-97 (2002)

MEDLINE 22105644

PUBMED 12110170

REFERENCE 7 (bases 1 to 1473)

AUTHORS Levitan, D., Yu, G., St George Hyslop, P. and Goutte, C.

TITLE APH-2/nicastrin functions in LIN-12/Notch signaling in the *Caenorhabditis elegans* somatic gonad

JOURNAL Dev. Biol. 240 (2), 654-661 (2001)

MEDLINE 21643937

PUBMED 11784090

REFERENCE 8 (bases 1 to 1473)

AUTHORS Maruyama, S., Hatakeyama, S., Nakayama, K., Ishida, N., Kawakami, K. and Nakayama, K.

TITLE Characterization of a mouse gene (Fbxw6) that encodes a homologue of *Caenorhabditis elegans* SEL-10

JOURNAL Genomics 78 (3), 214-222 (2001)

MEDLINE 21601157

PUBMED 11735228

REFERENCE 9 (bases 1 to 1473)

AUTHORS Cinar, H.N., Sweet, K.L., Hosemann, K.E., Earley, K. and Newman, A.P.

TITLE The SEL-12 presenilin mediates induction of the *Caenorhabditis elegans* uterine pi cell fate

JOURNAL Dev. Biol. 237 (1), 173-182 (2001)

MEDLINE 21409869

PUBMED 11518514

REFERENCE 10 (bases 1 to 1473)

AUTHORS Okochi, M., Eimer, S., Bottcher, A., Baumeister, R., Romig, H., Walter, J., Capell, A., Steiner, H. and Haass, C.

TITLE A loss of function mutant of the presenilin homologue SEL-12 undergoes aberrant endoproteolysis in *Caenorhabditis elegans* and increases abeta 42 generation in human cells

JOURNAL J. Biol. Chem. 275 (52), 40925-40932 (2000)

MEDLINE 20576248

PUBMED 11013240

REFERENCE 11 (bases 1 to 1473)

AUTHORS Wen, C., Levitan, D., Li, X. and Greenwald, I.

TITLE spr-2, a suppressor of the egg-laying defect caused by loss of sel-12 presenilin in *Caenorhabditis elegans*, is a member of the SET protein subfamily

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 97 (26), 14524-14529 (2000)

MEDLINE 20570513

PUBMED 11114162

REFERENCE 12 (bases 1 to 1473)

AUTHORS Zhang, D.M., Levitan, D., Yu, G., Nishimura, M., Chen, F., Tandon, A., Kawarai, T., Arawaka, S., Supala, A., Song, Y.Q., Rogaeva, E., Liang, Y., Holmes, E., Milman, P., Sato, C., Zhang, L. and St George-Hyslop, P.

TITLE Mutation of the conserved N-terminal cysteine (Cys92) of human presenilin 1 causes increased A beta42 secretion in mammalian cells but impaired Notch/lin-12 signalling in *C. elegans*

JOURNAL Neuroreport 11 (14), 3227-3230 (2000)

MEDLINE 20496269

PUBMED 11043553

REFERENCE 13 (bases 1 to 1473)

AUTHORS Yu, G., Nishimura, M., Arawaka, S., Levitan, D., Zhang, L., Tandon, A., Song, Y.Q., Rogaeva, E., Chen, F., Kawarai, T., Supala, A., Levesque, L., Yu, H., Yang, D.S., Holmes, E., Milman, P., Liang, Y., Zhang, D.M., Xu, D.H., Sato, C., Rogaev, E., Smith, M., Janus, C., Zhang, Y., Aebersold, R., Farrer, L.S., Sorbi, S., Bruni, A., Fraser, P. and St George-Hyslop, P.

TITLE Nicastrin modulates presenilin-mediated notch/glp-1 signal transduction and betaAPP processing

JOURNAL Nature 407 (6800), 48-54 (2000)

MEDLINE 20445163

PUBMED [10993067](#)
 REFERENCE 14 (bases 1 to 1473)
 AUTHORS Wittenburg,N., Bimer,S., Lakowski,B., Rohrig,S., Rudolph,C. and Baumeister,R.
 TITLE Presenilin is required for proper morphology and function of neurons in *C. elegans*
 JOURNAL Nature 406 (6793), 306-309 (2000)
 MEDLINE [20372200](#)
 PUBMED [10917532](#)
 REFERENCE 15 (bases 1 to 1473)
 AUTHORS Jacobsen,H., Reinhardt,D., Brockhaus,M., Bur,D., Kocyba,C., Kurt,H., Grim,M.G., Baumeister,R. and Loetscher,H.
 TITLE The influence of endoproteolytic processing of familial Alzheimer's disease presenilin 2 on abeta42 amyloid peptide formation
 JOURNAL J. Biol. Chem. 274 (49), 35233-35239 (1999)
 MEDLINE [20044792](#)
 PUBMED [10575009](#)
 REFERENCE 16 (bases 1 to 1473)
 AUTHORS Berezovska,O., Frosch,M., McLean,P., Knowles,R., Koo,E., Kang,D., Shen,J., Lu,F.M., Lux,S.E., Tonegawa,S. and Hyman,B.T.
 TITLE The Alzheimer-related gene presenilin 1 facilitates notch 1 in primary mammalian neurons
 JOURNAL Brain Res. Mol. Brain Res. 69 (2), 273-280 (1999)
 MEDLINE [99296661](#)
 PUBMED [10366748](#)
 REFERENCE 17 (bases 1 to 1473)
 AUTHORS Ray,W.J., Yao,M., Nowotny,P., Mumm,J., Zhang,W., Wu,J.Y., Kopan,R. and Goate,A.M.
 TITLE Evidence for a physical interaction between presenilin and Notch
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 96 (6), 3263-3268 (1999)
 MEDLINE [99179050](#)
 PUBMED [10077672](#)
 REFERENCE 18 (bases 1 to 1473)
 AUTHORS Westlund,B., Parry,D., Clover,R., Basson,M. and Johnson,C.D.
 TITLE Reverse genetic analysis of *Caenorhabditis elegans* presenilins reveals redundant but unequal roles for sel-12 and hop-1 in Notch-pathway signaling
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 96 (5), 2497-2502 (1999)
 MEDLINE [99162634](#)
 PUBMED [10051671](#)
 REFERENCE 19 (bases 1 to 1473)
 AUTHORS Hong,C.S., Caromile,L., Nomata,Y., Mori,H., Bredesen,D.E. and Koo,E.H.
 TITLE Contrasting role of presenilin-1 and presenilin-2 in neuronal differentiation in vitro
 JOURNAL J. Neurosci. 19 (2), 637-643 (1999)
 MEDLINE [99098950](#)
 PUBMED [9880584](#)
 REFERENCE 20 (bases 1 to 1473)
 AUTHORS Wu,G., Hubbard,E.J., Kitajewski,J.K. and Greenwald,I.
 TITLE Evidence for functional and physical association between *Caenorhabditis elegans* SEL-10, a Cdc4p-related protein, and SEL-12 presenilin
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 95 (26), 15787-15791 (1998)
 MEDLINE [99080092](#)
 PUBMED [9861048](#)
 REFERENCE 21 (bases 1 to 1473)
 AUTHORS Levitan,D. and Greenwald,I.
 TITLE Effects of SEL-12 presenilin on LIN-12 localization and function in *Caenorhabditis elegans*
 JOURNAL Development 125 (18), 3599-3606 (1998)
 MEDLINE [98384316](#)
 PUBMED [9716525](#)
 REFERENCE 22 (bases 1 to 1473)
 AUTHORS Berezovska,O., Xia,M.Q. and Hyman,B.T.
 TITLE Notch is expressed in adult brain, is coexpressed with presenilin-1, and is altered in Alzheimer disease

JOURNAL J. Neuropathol. Exp. Neurol. 57 (8), 738-745 (1998)
MEDLINE 98385443
PUBMED 9720489
REFERENCE 23 (bases 1 to 1473)
AUTHORS Li,X. and Greenwald,I.
TITLE Additional evidence for an eight-transmembrane-domain topology for Caenorhabditis elegans and human presenilins

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 95 (12), 7109-7114 (1998)
MEDLINE 98284066
PUBMED 9618547
REFERENCE 24 (bases 1 to 1473)
AUTHORS Davis,J.A., Naruse,S., Chen,H., Eckman,C., Younkin,S., Price,D.L., Borchelt,D.R., Sisodia,S.S. and Wong,P.C.
TITLE An Alzheimer's disease-linked PS1 variant rescues the developmental abnormalities of PS1-deficient embryos

JOURNAL Neuron 20 (3), 603-609 (1998)
MEDLINE 98198534
PUBMED 9539132
REFERENCE 25 (bases 1 to 1473)
AUTHORS Zhang,W., Han,S.W., McKeel,D.W., Goate,A. and Wu,J.Y.
TITLE Interaction of presenilins with the filamin family of actin-binding proteins

JOURNAL J. Neurosci. 18 (3), 914-922 (1998)
MEDLINE 98099802
PUBMED 9437013
REFERENCE 26 (bases 1 to 1473)
AUTHORS Mattson,M.P., Guo,Q., Furukawa,K. and Pedersen,W.A.
TITLE Presenilins, the endoplasmic reticulum, and neuronal apoptosis in Alzheimer's disease

JOURNAL J. Neurochem. 70 (1), 1-14 (1998)
MEDLINE 98082804
PUBMED 9422341
REFERENCE 27 (bases 1 to 1473)
AUTHORS Mattson,M.P. and Guo,Q.
TITLE Cell and molecular neurobiology of presenilins: a role for the endoplasmic reticulum in the pathogenesis of Alzheimer's disease?

JOURNAL J. Neurosci. Res. 50 (4), 505-513 (1997)
MEDLINE 98067216
PUBMED 9404712
REFERENCE 28 (bases 1 to 1473)
AUTHORS Li,X. and Greenwald,I.
TITLE HOP-1, a Caenorhabditis elegans presenilin, appears to be functionally redundant with SEL-12 presenilin and to facilitate LIN-12 and GLP-1 signaling

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 94 (22), 12204-12209 (1997)
MEDLINE 98004548
PUBMED 9342387
REFERENCE 29 (bases 1 to 1473)
AUTHORS Hutton,M. and Hardy,J.
TITLE The presenilins and Alzheimer's disease

JOURNAL Hum. Mol. Genet. 6 (10), 1639-1646 (1997)
MEDLINE 97444123
PUBMED 9300655
REFERENCE 30 (bases 1 to 1473)
AUTHORS Wong,P.C., Zheng,H., Chen,H., Becher,M.W., Sirinathsinghji,D.J., Trumbauer,M.E., Chen,H.Y., Price,D.L., Van der Ploeg,L.H. and Sisodia,S.S.
TITLE Presenilin 1 is required for Notch1 and D111 expression in the paraxial mesoderm

JOURNAL Nature 387 (6630), 288-292 (1997)
MEDLINE 97297761
PUBMED 9153393
REFERENCE 31 (bases 1 to 1473)
AUTHORS Baumeister,R., Leimer,U., Zweckbronner,I., Jakubek,C., Grunberg,J. and Haass,C.
TITLE Human presenilin-1, but not familial Alzheimer's disease (FAD) mutants, facilitate Caenorhabditis elegans Notch signalling

independently of proteolytic processing
JOURNAL Genes Funct. 1 (2), 149-159 (1997)
MEDLINE [98343909](#)
PUBMED [9680315](#)
REFERENCE 32 (bases 1 to 1473)
AUTHORS Hong, C.S. and Koo, E.H.
TITLE Isolation and characterization of Drosophila presenilin homolog
JOURNAL Neuroreport 8 (3), 665-668 (1997)
MEDLINE [97260623](#)
PUBMED [9106743](#)
REFERENCE 33 (bases 1 to 1473)
AUTHORS Berezovska, O., Xia, M.Q., Page, K., Wasco, W., Tanzi, R.E. and Hyman, B.T.
TITLE Developmental regulation of presenilin mRNA expression parallels notch expression
JOURNAL J. Neuropathol. Exp. Neurol. 56 (1), 40-44 (1997)
MEDLINE [97144360](#)
PUBMED [8990127](#)
REFERENCE 34 (bases 1 to 1473)
AUTHORS Levitan, D., Doyle, T.G., Brousseau, D., Lee, M.K., Thinakaran, G., Slunt, H.H., Sisodia, S.S. and Greenwald, I.
TITLE Assessment of normal and mutant human presenilin function in Caenorhabditis elegans
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 93 (25), 14940-14944 (1996)
MEDLINE [97121494](#)
PUBMED [8962160](#)
REFERENCE 35 (bases 1 to 1473)
AUTHORS Li, X. and Greenwald, I.
TITLE Membrane topology of the C. elegans SEL-12 presenilin
JOURNAL Neuron 17 (5), 1015-1021 (1996)
MEDLINE [97092712](#)
PUBMED [8938132](#)
REFERENCE 36 (bases 1 to 1473)
AUTHORS Levitan, D. and Greenwald, I.
TITLE Facilitation of lin-12-mediated signalling by sel-12, a Caenorhabditis elegans S182 Alzheimer's disease gene
JOURNAL Nature 377 (6547), 351-354 (1995)
MEDLINE [96032531](#)
PUBMED [7566091](#)

COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [U35660](#) and [AV179958.1](#). On Nov 21, 2002 this sequence version replaced [gi:17569442](#).
Summary: This gene sel-12, also known as sum-1, F35H12.3, XB535 or YK4554, maps at (X; -19.01). Its phenotype is suppressor/enhancer of lin-12, suppressor of multi-vulva phenotype, facilitator of notch-type receptors signaling. It encodes a presenilin, membrane protein facilitator of Notch receptors signaling. From Pfam homology, the product would be involved in intracellular signaling cascade and would localize in membrane.

According to the Worm Transcriptome Project, it is well expressed in L3, L4, adult and culminating in embryos [Kohara cDNAs]. Its sequence is defined by 11 cDNA clones.

Phenotype

[from C. elegans II book] Allele ar131: (previously known as sum-1) recessive suppressor of multivulva phenotype of lin-12 hypermorph n950; impenetrant egg laying defective in lin-12 (+) background. Three other alleles: ar133, ar171 (100% egg laying defective, ar171/Df similar, W225opal). Cloned: encodes predicted 467 aa protein, 9 transmembrane domains; related to human presenilin genes (S182) and to SPE-4. [Levitan and Greenwald 1995; Iva Greenwald]. Allele ar131, ar40.
[Levitan D] suppressor of multivulva phenotype.
Selected strains available from the CGC.
GS883 dpy-5(e61) sel(ar40)I; unc-32(e189) lin-12(n676n930)III

[Greenwald IS] DpyUnc. ar40 is a semi-dominant suppressor. At 25C ar40 suppresses the Egl phenotype of ne676n930. At 15C a high percentage of hermaphrodites have a 0 AC-Egl phenotype. ar40 suppresses proximal mitosis. ar40 does not suppress vulval lineage defects.

AN87 sel-12(ty11) X [Anna Newman, Nese Cinar, EMS] Egl. Premature stop codon.

RNA interference results:

[J.Ahringer 2003] No obvious phenotype (by feeding genomic PCR product JA:F35H12.3). Warning: this double stranded RNA may also interfere with gene XB537.

Function

Protein properties: [GB:AF171064] function: facilitator of Notch receptors signaling.

membrane protein similar to Homo sapiens PS1 and PS2.

[WormBase] The sel-12 gene encodes a ortholog of human PS1, which when mutated leads to type 3 Alzheimer disease (OMIM:104311); it is also homologous to PS2, which when mutated leads type 4 Alzheimer disease (OMIM:600759).

Expression

The expression profile for the gene, derived from the proportion of animals at each stage in each Kohara library is: embryos 76%, L1 or L2 larvae 1%, L3 to adult 22%.

In situ hybridisation pictures to all stages of development are available from Kohara NextDB.

For a detailed expression pattern description, see Wormbase Expr1288, Expr1609.

Interactions

This gene interacts with:

gene spr-1: spr-1 loss of function suppresses Egl of sel-12.

protein LIN-12.

protein SEL-10CO.

This complete mRNA is 1473 bp long. Its sequence exactly matches the genome. The premessenger has 7 exons. It covers 2.42 kb on the WS97 genome. It is transplanted to SL1. The protein (444 aa, 50.0 kDa, pI 6.7) contains one Presenilin motif. It also contains at least 8 transmembrane domain, a prenylation domain, an ER membrane domain [Psort2]. It is predicted to localise in the plasma membrane [Psort2]. Taxblast (threshold 10^{-3}) tracks ancestors down to eukaryota.

COMPLETENESS: full length.

FEATURES

source

Location/Qualifiers

1..1473

/organism="Caenorhabditis elegans"

/mol_type="mRNA"

/db_xref="taxon:6239"

/chromosome="X"

/map="X;-19.01 cM (interpolated genetic position)"

/map="X;-18.80 cM (measured genetic position)"

/map="X; covering 2422 bp, from base 906456 to 908879 on genome release WS97"

/clone="Primers to amplify the CDS (3999 bp, Stop included): ATGCCTTCCACAAGGAGAC (T=57.6),

TTAATATAATAAACACTTTTGAGAGACTTG (T=55.2). Complete CDS clones: AF171064, U35660, yk221d3. Recommended clone (from the Kohara collection): yk221d3. Other clone(s):

yk674e3, yk499e3, yk400e8, yk600e12, yk216e1, yk231a7, yk573h4, yk452b9. for edited clone sequences see www.wormgenes.org

/clone_lib="Kohara embryonic lambda gt11 library: yk221d3, yk674e3, yk499e3, yk400e8, yk600e12, yk216e1, yk573h4, yk452b9; Kohara mixed stage library, from him-8 strain,

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 /locus_tag="XB535"
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 /locus_tag="XB535"
 /note="Intron length 70 bp, type gt_ag"
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 /note="Intron length 304 bp, type gt_ag"
exon 246..455
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 /locus_tag="XB535"
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 /locus_tag="XB535"
 /note="Intron length 45 bp, type gt_ag"
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 /note="Exon 4 length 320 bp"
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 /note="Intron length 61 bp, type gt_ag"
exon 776..859
 /gene="sel-12"
 /locus_tag="XB535"
 /note="Exon 5 length 84 bp"

containing 15-30% males: yk231a7; gb: AF171064, U35660"

gene 1..1473
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 /locus_tag="XB535"
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 /db_xref="AceView/WormGenes:sel-12"
 /db_xref="LocusID:180441"

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 /codon_start=1
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 LFVISVWDLVAVLTPKGPLRYLVETAQERNEPIFPALIIYSSGVIYPYVLVTAVENTTD
 PREPTSSDSNTSTAFPGEASCSETPKRPKVKRIPQKVQIESNTTASTTQNSGVRVER
 ELAAERPTVQDANFHRHEEEERGVLGLGDFIFYSVLLGKASSYFDWNTTIACYVAIL
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misc_feature 403..453
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misc_feature 496..546
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misc_feature 580..630
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 /locus_tag="XB535"
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 /gene="sel-12"
 /locus_tag="XB535"
 /note="Intron length 422 bp, type gt_ag"
exon 1067..1473
 /gene="sel-12"
 /locus_tag="XB535"
 /note="Exon 7 length 407 bp"
3'UTR 1336..1473
 /gene="sel-12"
 /locus_tag="XB535"
 /note="The 3' UTR contains 138 bp followed by the polyA.
 The standard AATAAA polyadenylation signal does not occur,
 but the variant ATTAAA is seen about 15 bp before the
 polyA."
 /evidence=experimental
polyA_signal 1459..1464
 /gene="sel-12"
 /locus_tag="XB535"
 /note="variant attaaa"
polyA_site 1473
 /gene="sel-12"
 /locus_tag="XB535"
 /note="PolyA visible in U35660, yk452b9"
 /evidence=experimental

BASE COUNT 381 a 313 c 312 g 467 t
 ORIGIN

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